

A. AMENDMENTS TO THE CLAIMS

Item 2: The Examiner has stated that the substitute specification includes a complete set of claims as originally filed and that if the substitute specification were entered the application would then contain two sets claims. Applicant herewith submits a new substitute specification excluding the claims and abstract to be considered for entry by the Examiner.

Please amend the claims as follows:

1-4. (Cancelled)

5. (Presently Amended) A compound of formula II:

B-R-A-NHN=C(R¹R²) II

or a derivative thereof, wherein:

A is NH(C=O)-, NH(C=S)-, NHNH(C=O)-, or NHNH(C=S)- or a direct bond to R;

B is an amino or thiol reactive moiety;

R is an aliphatic divalent group having any combination of the following groups, which are combined in any order: cycloalkylene, C(R¹⁰)₂, -C(R¹⁰)=C(R¹⁰)-, >C=C(R¹²)(R¹³), >C(R¹²)(R¹³), -C≡C-, O, S(G)_a, P(J)_b(R¹⁰), P(J)_b(LR¹⁰), N(R¹⁰), >N⁺(R¹²)(R¹³) and C(L); where a is 0, 1 or 2; b is 0, 1, 2 or 3; G is O or NR¹⁰; J is S or O; and L is S, O or NR¹⁰; each R¹⁰ is a monovalent group independently selected from hydrogen and M¹-R¹⁴; each M¹ is a divalent group independently having any combination of the following groups, which groups are combined in any order: a direct link, arylene, heteroarylene, cycloalkylene, C(R¹⁵)₂, -C(R¹⁵)=C(R¹⁵)-, >C=C(R¹²)(R¹³), >C(R¹²)(R¹³), -C≡C-, O, S(G¹)_a, P(J)_b(R¹⁵), P(J)_b(LR¹⁵), P(J)_b(L¹R¹⁵), N(R¹⁵), N(COR¹⁵), >N⁺(R¹²)(R¹³) and C(L¹); where a is 0, 1 or 2; b is 0, 1, 2 or 3; G¹ is O or NR¹⁵; J is S or O; and L¹ is S, O or NR¹⁵; R¹⁴ and R¹⁵ are each independently selected from the group among hydrogen, halo, pseudohalo, cyano, azido, nitro, SiR¹⁶R¹⁷R¹⁸, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclalkyl, heterocyclalkenyl, heterocyclalkynyl,

hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and NR¹⁹R²⁰; R¹⁹ and R²⁰ are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl; R¹² and R¹³ are selected from (i) or (ii) as follows: (i) R¹² and R¹³ are independently selected from among hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or (ii) R¹² and R¹³ together form alkylene, alkenylene or cycloalkylene; R¹⁶, R¹⁷ and R¹⁸ are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and NR¹⁹R²⁰; and

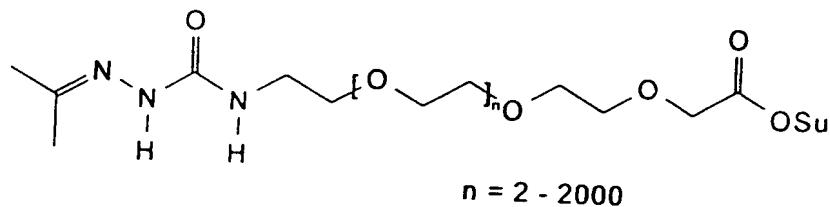
R¹¹-R¹⁰, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹ and R²⁰ can be substituted with one or more substituents each independently selected from Z, wherein Z is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy, S(O)_hR³⁰, NR³⁰R³¹, COOR³⁰, COR³⁰, CONR³⁰R³¹, OC(O)NR³⁰R³¹, N(R³⁰)C(O)R³¹, alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocyclyloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocabamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido; h is 0, 1 or 2; and R³⁰ and R³¹ are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylarylarnino, diarylamino and arylamino;

R¹ is a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms; and

R^2 is a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms.

6. (Presently Amended) The compound of claim 5, wherein R is further comprises, or is a combination of, a saturated straight chain of 1 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms.

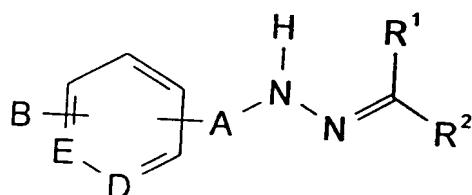
7. (Presently Amended) The compound of claim 5-6 that is:



8-34. (Cancelled)

35. (Currently amended) A method of crosslinking a natural or synthetic biological molecule, comprising:

(i) preparing a conjugate of formula Va:



Va

or a derivative thereof, wherein:

A is $\text{NH}(\text{C}=\text{O})$, $\text{NH}(\text{C}=\text{S})$, $\text{NH}(\text{C}=\text{NH})$, $\text{NHNH}(\text{C}=\text{O})$, $\text{NHNH}(\text{C}=\text{S})$, $\text{NHNH}(\text{C}=\text{NH})$ or a direct bond;

B is a natural or synthetic biological molecule;

D is a carbon or nitrogen atom;

E is a carbon or nitrogen atom;

R¹ is hydrogen or a saturated straight chain of 1 to 12 carbon atoms; and

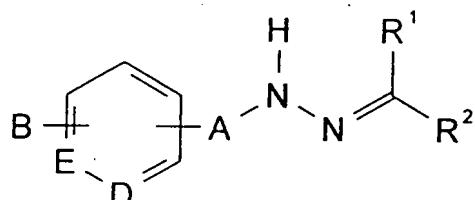
R² is hydrogen or ~~a saturated~~ a saturated straight chain of 1 to 12 carbon atoms; and

(ii) applying the conjugate to a surface wherein the surface has at least one carbonyl moiety for a time and under conditions such that the hydrazine moiety of the conjugate reacts with the amino or one carbonyl moiety of the surface forming a hydrazone bond thereby crosslinking the natural or synthetic biological molecule to the surface.

36-37. (Cancelled)

38. (Currently Amended) A method of crosslinking a natural or synthetic biological molecule, comprising:

(i) preparing a conjugate of formula Va:



Va

or a derivative thereof, wherein:

A is NH(C=O), NH(C=S), NH(C=NH), NHNH(C=O), NHNH(C=S), NHNH(C=NH) or a direct bond;

B is a natural or synthetic biological molecule;

D is a carbon or nitrogen atom;

E is a carbon or nitrogen atom;

R¹ is hydrogen or a saturated straight chain of 1 to 12 carbon atoms; and

R² is hydrogen or a saturated straight chain of 1 to 12 carbon

atoms; and

(ii) mixing the conjugate with a second natural or synthetic biological molecule, wherein the second natural or synthetic biological molecule has at least one carbonyl moiety, for a time and under conditions such that the hydrazine moiety of the conjugate reacts with the carbonyl moiety of the second natural or synthetic biological molecule forming a hydrazone bond thereby crosslinking the natural or synthetic biological molecule to the second natural or synthetic biological molecule.

39-48. (Cancelled)

49. (Original) The compound of claim 5, wherein B is an amino reactive moiety selected from succinimidyl ester, hydroxybenzotriazolyl ester, or pentafluorophenol ester.

50-51 (Cancelled)

52. (Original) The compound of claim 5, wherein B is a thiol reactive moiety selected from maleimido, α -bromoacetyl, α -bromoacetamido, α -bromoacetamide or pyridyldisulfide.

53. (Cancelled)

Applicant submits that to the best of his knowledge these amendments do not add new matter to the specification.